



Atty Dkt. No. 112461-016

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Patent Application of: )  
For:      Joanne Y. H. Kwak-Kim et al. )  
              DIAGNOSIS AND TREATMENT )  
              OF INFERTILITY )  
Serial No. 10/651,690 )  
Filed:      August 28, 2003 )  
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Art Unit: 1644 )  
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CERTIFICATE OF MAILING

I hereby certify that this paper is being deposited  
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Tin-Chuen Young

DECLARATION OF DR. KWAK-KIM UNDER 37 C.F.R. §131

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

I, Joanne Young Hee Kwak-Kim, M.D., aver as follows:

1. I am over the age of twenty-one years and make these statements from my own personal knowledge.
2. I obtained an M.D. degree in 1984 from the College of Medicine, Yonsei University Seoul, Korea and an M.S. degree in 1987 from the Graduate School of Yonsei University.
3. I currently hold the position of the Assistant Chair, Department of Obstetrics and Gynecology; and the Medical Director, the Clinics at Rosalind Franklin University; and the Director, Women's Health Division, University Clinics; and Associate Professor, Department of Obstetrics and Gynecology and the Department of Microbiology and Immunology of the Rosalind Franklin University of Medicine and Science (formerly known as Finch University of Health Sciences)/The Chicago Medical School.

4. I am a joint inventor of the above-captioned patent application.
5. I understand that certain claims of this patent application have been rejected by the United States Patent and Trademark Office in view of United States Patent Application Publication No. US 2001/0021380A1 in combination with other references. This U.S. Publication published on September 13, 2001, and claims priority from numerous patent applications the earliest of which was filed on April 19, 1999 ("Critical Date").
6. Prior to the Critical Date, I had planned to study the affect on reproductive outcomes, in subjects with a history of recurrent spontaneous abortions or implantation failures, of adjusting the balance of T helper 1 (Th1) and T helper 2 (Th2) immune responses in the subject. In particular, I determined to decrease the ratio of Th1 immune response to Th2 immune response by either (a) down regulating the Th1 immune response, (b) by up regulating the Th2 immune response or (c) by both down regulating the Th1 immune response while up regulating the Th2 immune response.
7. The ratio of the Th1 to Th2 immune responses can be measured by absolute cell counts or percentage of Th1 cells to Th2 cells. Th1 cells are the activated T-cells expressing Th1 cytokines such as IL-1, IL-2, and TNF- $\alpha$ . Th2 cells are the activated T-cells expressing Th2 cytokines such as IL-4, IL-5, IL-6 and IL-10. The ratio of the Th1 to Th2 immune responses can also be determined by calculating a ratio of any one of the Th1 cytokines to any one of the Th2 cytokines.
8. One method I contemplated to reduce the Th1 count was to administer to a subject, prior to conception by the subject, a TNF- $\alpha$  antagonist. TNF- $\alpha$  antagonist may be of several types including antibodies, soluble receptors, and chemical compounds. I contemplated using several commercially available TNF- $\alpha$  antagonists and TNF- $\alpha$  antagonists that were undergoing

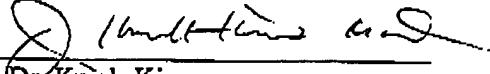
an FDA approval process in the hope of becoming commercially saleable. Examples of antibody type and soluble receptor-type TNF- $\alpha$  antagonists included, but were not limited to: (1) infliximab (antibody-type) (2) entanercept (soluble receptor-type), (3) D2E7 (antibody-type) (4) CDP571 (antibody-type) and (5) CDP870 (antibody-type).

9. I contemplated administering the TNF- $\alpha$  antagonist by any medically suitable route of administration.

10. After conceiving of these concepts I worked on them diligently from prior to the Critical Date up to the time of filing the above-captioned patent application.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, I acknowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code and may jeopardize the validity of the application or any patent issuing thereon.

Date: August 29, 2005

BY   
Dr. Kwak-Kim